

MEASLES OUTBREAK RESPONSE PLAN

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Scope and Purpose

Although many of the procedures discussed in this plan are applicable to the investigation of other infectious diseases, this plan details the response to a measles outbreak specifically. It is the intent of this plan to be fully compatible with CDC recommendations for measles investigation and control while applying those recommendations to procedural response by NDDoH Disease Control Division and the Emergency Preparedness and Response Section. Parts of this response plan are dependent on other response plans (e.g., Isolation and Quarantine, Community Containment). Those plans are referenced when appropriate.

Agent and Illness

Measles is a viral illness (paramyxovirus) that is no longer endemic in the Western Hemisphere, but remains common in much of the world. Outbreaks continue to occur in the United States annually. Any cases identified in North Dakota will have been either imported by persons who have recently lived or traveled outside the United States, or by persons who had contact to an ongoing outbreak in some other part of the U.S. The disease is capable of causing sustained outbreaks, but outbreaks in the US tend to be small due to the relatively high vaccine coverage and high vaccine efficacy. Measles is unlikely in persons who have been vaccinated and very unlikely in persons who have had two documented vaccinations¹.

The disease is potentially severe, so disease control efforts must be aggressive. Approximately 20% of cases will be hospitalized. The most common complications are pneumonia and otitis media. Encephalitis is uncommon but can be fatal or cause permanent neurological disability. A rare late neurological complications (sub-acute sclerosing panencephalitis) can cause death years after the acute illness. No specific treatment for measles exists. Care is supportive with management of complications.

The illness is characterized by initial onset of fever, malaise, cough, coryza, and conjunctivitis. A maculopapular rash, usually beginning on the face then becoming generalized, appears between days 3 and 7 after onset of illness². The average incubation period for measles is 12 days from exposure to prodrome and 14 days from exposure to rash (range of 7–21 days). Period of infectivity begins as early as 4 days before onset of rash and may continue until 4 days after onset of rash. That is, cases are likely to be infectious during much or all of the prodromal period prior to rash onset. Cases which are not epidemiologically linked to a known case are very unlikely to be recognized as possible measles prior to

Measles Statistics

- Symptoms: fever, malaise, cough, coryza, conjunctivitis and maculopapular rash.
- Incubation period: 7-21 days (average 12 days from exposure to illness onset)
- Duration: Prodrome (pre-rash) lasts from 2-8 days. Rash typically lasts from 4 to 7 days. Cough can persist for 2 weeks
- Hospitalization: 20%
- Period of infectivity: 4 days before rash onset to 4 days after rash onset.
- Susceptibility: Born in 1957 or later and unvaccinated
- Mode of Spread: airborne, droplet, secretions, fomites
- Diagnosis: a) IgM (70% positive at time of rash onset, 100% by four days post rash onset); b) acute and convalescent titers; c) viral isolation; d) PCR
- Pre-exposure vaccine efficacy: 94% one dose, 99+% two doses
- Isolation and quarantine: Yes
- Post-exposure prophylaxis: 72 hour window for vaccine but limited efficacy; 5 day window for IG but limited efficacy.
- Treatment: Supportive

¹ US studies suggest that 94% of persons vaccinated with a single dose and 99+% of persons vaccinated with a second dose will be immune. Some Canadian studies have found lower rates of immunity.

² Failure to develop rash is exceedingly rare in immunocompetent individuals.

rash onset and diagnosis is often delayed for unlinked cases, so unlinked cases are particularly likely to have many contacts before they are isolated. Measles is highly contagious and spreads via droplet and airborne routes and by direct contact with secretions, including secretions on fomites. It has been estimated that 90% of non-immune individuals can be expected to develop disease following exposure³. Secondary cases can occur in hospitals from patients admitted with acute illness, and transmission in waiting rooms of clinics and emergency rooms is common.

Case Definition

Case definitions below, which are consistent with those published in the MMWR from CSTE, are taken from <http://www.cdc.gov/vaccines/pubs/surv-manual/chpt07-measles.html>.

Suspected:

Any febrile illness that is accompanied by rash and that does not meet the criteria for probable or confirmed measles or any other illness.

Probable:

- In the absence of a more likely diagnosis, an illness characterized by
 - Generalized rash lasting ≥ 3 days; and
 - Temperature $\geq 101^{\circ}\text{F}$ or 38.3°C ; and
 - Cough, coryza, or conjunctivitis; and
- No epidemiologic linkage to a confirmed case of measles; and
- Noncontributory or no serologic or virologic testing.

Confirmed:

- Laboratory confirmation by any of the following
 - Positive serologic test for measles immunoglobulin M antibody;
 - Significant rise in measles antibody level by any standard serologic assay;
 - Isolation of measles virus from a clinical specimen; or
 - Detection of measles-virus specific nucleic acid by polymerase chain reaction

Note: A laboratory-confirmed case does not have to have generalized rash lasting ≥ 3 days; temperature $\geq 101^{\circ}\text{F}$ or 38.3°C ; cough, coryza, or conjunctivitis.

OR

- An illness characterized by
 - Generalized rash lasting ≥ 3 days; and
 - Temperature $\geq 101^{\circ}\text{F}$ or 38.3°C ; and
 - Cough, coryza, or conjunctivitis; and
 - Epidemiologic linkage to a confirmed case of measles

Laboratory

Measles serology is usually employed to confirm cases and testing is available in the NDDoH Division of Laboratory Services. Positive serology is defined as detection of IgM antibodies, which begin to rise at about the time of rash onset and can persist for one to two months. (At the time of rash onset, 70% of

³ Exposure exists on a continuum with non-immune persons more likely to become ill due to close contact than more casual contact.

cases will have a positive IgM.) Alternatively, diagnosis can be made by detection of a rise in IgG between acute and convalescent titers taken 14 to 30 days apart. IgG levels do not begin to rise until 5 to 10 days post rash onset, meaning, acute titers should optimally be drawn before five days post rash onset.

Vaccination also causes an increase in IgM and IgG, but titers do not typically begin to rise until 8 to 21 days post vaccination. A positive serology cannot be relied upon for diagnosis between 6 and 45 days post vaccination. Viral isolation of a wild type measles virus would be needed to confirm the diagnosis in a person whose IgM could be elevated due to vaccination. (However, if the IgM titer is negative greater than 72 hours post onset of rash illness, measles is ruled out.) Vaccination should not be withheld to preserve the capability for serological confirmation, even if the person is more than 72 hours post exposure. In practice, an illness which meets clinical case definition in a person with an epidemiological link to a confirmed case is considered a confirmed case. However, a measles-like illness with fever, rash and malaise can occur about one week post-vaccination and usually lasts 1-2 days (15% of vaccinees develop fever, which can be high, and 5% develop a transient rash). Although febrile rash illness due to vaccination will generally not meet the case definition for rash duration, it can be confused with measles caused by a wild virus. This is further complicated by the fact that a case of measles from the wild virus developing following vaccination is often milder than usual cases and may not meet the clinical case definition. Consequently, viral isolation and typing should be performed to confirm a case of measles which does not meet case definition post-vaccination for exposure.

Upon first contact with a potential measles case, both IgM and IgG should be tested, and a specimen should be taken for potential viral isolation. A negative IgM drawn during the first 72 hours after rash onset does not exclude measles; consequently, suspect cases with a negative IgM drawn within the first 72 hours post rash onset should have repeat testing after 72 hours. All cases should have a positive IgM by 72 hours post rash onset. However, both false negative and false positive tests can occur.

False positives for IgM are more likely in the presence of rheumatoid factor and may be positive in patients with parvovirus B19, rubella, roseola or dengue. Each of these viruses is also associated with a rash that can be confused with measles, although not all have a typical measles-like rash. When results are equivocal, diagnosis may be confirmed by four fold rise in IgG titer between acute and convalescent sera, viral isolation or PCR. However, selection and interpretation of all tests is dependent on timing of specimen collection and whether vaccine was recently given.

During an outbreak, the number of febrile rash illnesses reported to the state by providers or health care facilities is likely to increase substantially, and many of these rashes will not be measles. Likewise, in a sizeable outbreak, some atypical measles cases may occur, for example, cases modified by post-exposure prophylaxis.

[Specimen Collection](#)

Collect specimens for both serology and viral isolation simultaneously. Sufficient blood should be taken to test for both measles and rubella if the case is sporadic (i.e., not epi-linked to a known case).

[Serology](#)

Blood, 3-5 ml collected in clot separator tubes (should be sufficient for both measles and rubella if needed)

- 1) IgM serology: Collect ASAP and, if negative, repeat at >72 hours after rash onset. [*IgM is detected for at least 28 days after rash onset.*]

- 2) IgG serology: Collect paired sera.
 - a. **Acute:** ASAP after rash onset (7 days at the latest);
 - b. **Convalescent:** 14–30 days after first specimen.

Viral Isolation

Throat (and/or nasopharyngeal) swabs are the preferred clinical samples. A urine sample as well is desirable.

- Preferred collection is within 3 days of rash onset, but may be collected up to 7 days post rash onset.
- Use Dacron or synthetic swab placed in Viral Transport Media (VTM).
- Keep all specimens on wet ice or at 4°C until shipment.
- Ship as soon as possible on cold packs.

If not shipped within 48 hours refer to CDC guidance or contact state lab for proper procedure in freezing specimens.

PCR

PCR is not performed by the state lab in North Dakota. Specimens will need to be sent to Minnesota. A buccal swab, nasopharyngeal aspirate or swab, or urine specimen is needed. Swabs should be synthetic. Volume requirement is 250µL (0.25 cc). The specimen should be stored in 2mL viral transport media at 4°C if shipping within 24 hours and ship on cold packs. If shipping is delayed, freeze at -70°C and transport frozen.

Specimen Transport

One of two options is used to transport most specimens to the state lab, as follows:

1. FedEx with next day delivery
2. Courier - The courier service transports specimens to our lab Monday – Friday from 14 major ND hospitals. Specimens arrive at our lab late at night same day or very early in the morning the next day.

In situations where commercial transport is not fast enough, alternate arrangements will have to be made by the field investigators. A local responder can be dispatched to the lab with the specimens, or if sufficient resources are not available locally, field investigators can contact Disease Control or the DOC to request assistance with immediate specimen transport. Since measles has no definitive treatment and preventive measures can be taken without diagnosis confirmation, urgent diagnosis of a measles case would not warrant transport by state police or civil air patrol.

Outbreak surveillance and Population Preventive Measures

Measles is a reportable condition in North Dakota, but because the disease is not endemic, only a single case of measles has been identified in North Dakota in over 20 years⁴, and many clinicians have never seen a case. Consequently, recognition of an outbreak may be delayed. Identification of an initial case in North Dakota would be expected to occur in one of the following ways:

1. Recognition and report by a clinician of a compatible illness in a patient with or without history of exposure to a measles case.
2. Notification of NDDoH of a contact in North Dakota to a known case in another state or on public conveyance.

⁴ The case was diagnosed in 2011 in a person born before 1957 who was exposed on a commercial air flight to a domestic outbreak case.

3. Evidence of increase in febrile rash illness noted on syndromic surveillance⁵ found to be measles on investigation.
4. School report of children with febrile rash illness or increased absenteeism reportedly due to febrile rash illness found to be measles on investigation.

During a measles outbreak, clinics, hospitals and public health agencies in the outbreak community would be contacted and asked to report all cases of febrile rash illness. Some clinics may be called daily depending on the circumstances of the outbreak. Likewise, depending on age of the case and suspected risk factors for transmission, schools or day cares in the impacted area may be notified and asked to report all cases of fever and rash illness. In some outbreaks, review of emergency and laboratory records in health care facilities in or near the outbreak area and in major referral centers outside the outbreak area may be considered to identify previously unidentified cases.

[Response to Request for Measles Evaluation](#)

When a patient is referred to public health because concern about measles, case history needs to be obtained to determine whether the person 1) meets the clinical case definition, 2) is epidemiologically linked to a known case of measles or has a history of recent travel to a place where measles contact would be possible (US outbreak area or international travel), and 3) has evidence of measles immunity. Not all persons with an acute febrile rash illness should have serological testing for measles due to the risk of false positive serology. The decisions to obtain testing will be affected by the individual case circumstances, but the information below offers guidelines:

- All persons with an epidemiological link to a known case who present with febrile rash illness, regardless whether the case meets clinical case definition or whether the person has a vaccination history, should have serology and viral isolation specimens taken. A positive serology may be considered to confirm the diagnosis. If serology is negative, viral isolation should be considered to rule out a false negative.
- Persons with a history of travel where exposure is possible should be tested if they meet the clinical case definition. If they do not meet the clinical characteristics of the case definition, testing may still be reasonable, particularly if the person is not vaccinated, but viral isolation should be considered only for positive results.
- For persons with no risk factors for measles exposure who have a clinical illness which is consistent with the case definition and have not been vaccinated, testing may be reasonable, but viral isolation should be used to confirm the diagnosis.
- For persons, who have typical clinical features of measles but no risk factors and a confirmed vaccination history are very unlikely to have measles and testing is likely not indicated.
- For persons who have a clinical history not consistent with the case definition and no risk factors are very unlikely to have measles and testing is likely not indicated.

[Initial Response to a Positive Measles Serology](#)

For sporadic cases (not epidemiologically linked to a known case) viral isolation is always reasonable to confirm that a measles outbreak is occurring. Certainly any time there is reason to believe that a false positive is reasonably likely, viral isolation should be conducted. A false positive should be considered reasonably likely when the case does not meet the clinical definition of measles, the person has no risk factors for exposure or the person has a confirmed vaccination history. Voluntary isolation would be recommended for laboratory positive cases which are considered low risk, but additional control actions

⁵ Note: At the time of this writing, syndromic surveillance in North Dakota is not available due to upgrade process.

would likely be delayed pending additional confirmatory testing. If the likelihood of measles is high, isolation of the case and contact tracing with vaccination and quarantine would be initiated immediately.

Response Activation

Department Operations Center (DOC)

An outbreak which consists of a single measles case that can be quickly contained would not result in activation of the DOC. If more than one case is identified, the DOC would likely be activated. Examples of assistance likely to be requested from the DOC include:

1. Activation of hotline
2. Activation of HAN
3. Statewide videoconferencing support
4. Personnel assistance for tasks in Disease Control (data entry, data management/analysis, vaccine record research)
5. Additional NDDoH personnel for field assignment (e.g., creation of additional two person investigation teams)
6. Assistance with isolation and quarantine (e.g., legal, local management assistance).
7. Vaccine management and cold chain
8. Assistance with mass vaccination
9. Social distancing policy
10. Resources and logistics

Role of LPHU

Some activities would be the primary responsibility of the local public health agency; however, some local jurisdictions have very little public health capacity, so additional assistance may have to come from the state or from other local jurisdictions. Tasks which would fall to local public health include:

1. Managing isolation and quarantine, including mandatory orders and ensuring persons in voluntary or mandatory confinement have their needs met;
2. Case investigation teams – Local public health would potentially be called upon to supply personnel to assist with case investigation and contact tracing. LPH may be a ready source of nursing personnel who can obtain laboratory specimens and administer vaccine, preferably at the time of initial contact, to persons who were potentially exposed (this would require portable cold chain capability).
3. Mass vaccination clinics – In difficult to control outbreaks or in outbreaks involving schools, mass vaccination clinics may be necessary. This would be a primary responsibility of LPH.

Inter-State and Federal Interactions

NDDoH would notify CDC of any confirmed cases of measles in the state. NDDoH would look to CDC for advanced laboratory services (e.g., genetic linkage to outbreaks in other states), administrative approval for funds expenditure (e.g., use of federal vaccine for outbreak control), and expert consultation. It is expected that an in-state federal response would not be mounted unless the outbreak was large and the state was having difficulty getting it under control.

Cases which may have been infectious on a commercial air flight or other interstate transportation vehicle would result in a notification of the nearest quarantine station (Minneapolis <http://www.cdc.gov/quarantine/stations/minneapolis.html>, (612) 725-3005) for assistance with contact

tracing. Any potential contacts identified as residents of other states would be referred to the state department of health for that state for further follow-up.

Communicating with the Health Care System

Once an initial case of measles is identified in the state, all clinical providers, hospitals and public health agencies in the state would be notified of the illness. This notification would include the following information:

- Review of measles signs and symptoms, prevention and control;
- Disease management and potential complications;
- Outbreak overview including patient age, sex, where presumed exposure occurred (e.g., city, state, venue), city of residence and other sites where patient may have been while contagious;
- Instructions for immediate reporting by providers to public health re suspect cases prior to laboratory confirmation;
- Laboratory diagnosis requirements and directions to send specimens to state lab rather than out-of-state to reference labs;
- Recommendations for vaccination review of patient population and vaccination of both children and adults who do not have documentation of up-to-date (see Attachment A) vaccination⁶;
- Procedures for reporting adverse reactions to vaccination;
- Actions needed to prevent spread in emergency rooms and clinics⁷.

In addition, all health care facilities would be asked to review vaccination records of employees and require all persons without contraindications to have two documented doses of MMR. During periods of ongoing transmission, health care workers with contraindications to vaccination should be assigned away from outpatient work areas (ER, clinics) and hospital wards with known cases.

Communicating with the Public

Identification of measles anywhere in the state would result in public information releases alerting the population to the outbreak and asking them not to take family members with febrile rash illnesses to clinics or emergency rooms without alerting facilities before arrival.

Additional information provided to the public would include:

- Description of disease and manifestations;
- What to do and not to do if a person becomes ill with rash and fever;
- Personal exposure assessment and risk reduction;
- When a person needs additional vaccination;
- Actions to be taken by pregnant women, immunocompromised individuals and infants less than 6 months who cannot be vaccinated;
- How to access vaccination (locations, times);
- School exclusion criteria⁸.

⁶ At least in a large community, this should not be viewed as an outbreak control strategy. General population vaccination during measles outbreaks have not been demonstrated to help control the outbreaks.

⁷ Since measles is potentially contagious for four days prior to rash onset, all febrile illnesses should be screened away from the waiting area; however, care should be taken that persons with febrile rash illness are not be cohorted together since some may and some may not have measles.

⁸ The State Health Officer has authority to exclude a child from a school in order to control an outbreak of infectious disease (N.D.C.C 23-07-17).

Communicating with Schools

During an outbreak, schools may be asked to

- Exclude any child or employee that does not have written proof of up-to-date measles vaccination (see Attachment A);
- Immediately report any known cases of fever with rash illness and exclude the child from school;
- Close – although unlikely, if an outbreak is sustained and a school is considered an important location for continued transmission, this may be considered.

Disease Investigation

During a known outbreak, any febrile rash illness occurring in the outbreak area⁹ should be considered a potential measles case and reported immediately to public health¹⁰. However, even a relatively small outbreak could generate dozens of reports of febrile rash illness, most of which are not measles. In large outbreaks it may be necessary to target resources (e.g., more detailed investigation) on populations which are likely to be at risk. Pending laboratory results, a person with rash illness who is not known to be a contact of a confirmed measles case should be asked to voluntarily isolate themselves through at least four days after onset of rash. If the serology is negative but the specimen was drawn during the first 72 hours after rash onset, the person would not be released from isolation until a subsequent test taken after 72 hours post rash onset has returned negative. Persons with rash illness, even if atypical, who are known contacts of a confirmed case would be treated as presumptive measles until proven otherwise.

Attachment 2 shows a contingency table used to identify case status based on epidemiological, laboratory and clinical information. The table was taken from the CDC document *Manual for the Surveillance of Vaccine-Preventable Diseases (5th Edition, 2012)*.

Evaluation of Cases and Contacts

Cases of measles and their contacts need to be interviewed to collect basic information for disease control. Standard forms must be used which have been adopted for that specific outbreak investigation. These will be provided by Disease Control to field investigators and, at a minimum, will include the data elements recommended by CDC. In many instances, additional data will be collected specific to the outbreak and currently known risk factors for illness. Attachment 3 lists the data likely to be collected. Investigators should carry a calendar with them which should be used to assist the interviewee to remember specific activities, locations and times on specific dates. Whenever possible, case interviews should be done with the case. If this not possible, due to severity of illness, inability to provide accurate information (e.g., young child, dementia), or death, family members most likely to be able to provide the needed information should be interviewed. Whenever possible, case data should be collected in person since it is difficult to collect detailed exposure data over the phone. Contact interviews can be done over the phone, but in person interviews are preferred; if vaccination is required, an on-site visit is indicated in any case. Contacts should be carefully interviewed regarding the nature of any suspected exposure. Although highly contagious, intimate exposures or exposures in schools, day cares and

⁹ In some outbreaks, the entire state may be considered the outbreak area. In other situations, e.g., an outbreak among an immigrant population in Fargo, the risk area may be considered to be much smaller. Contact history may substantially impact this determination.

¹⁰ Rash can be more difficult to detect in dark-skinned individuals. The typical measles rash can be seen and felt in persons with dark skin, but will not be as immediately obvious, the extent and nature of the rash may be difficult to determine (more difficult to tell if typical or atypical), and the rash may be missed altogether.

prisons are more likely to result in transmission than more casual exposures. Attachment 4 lists criteria for determination of exposure.

Once exposure status is determined from history, susceptibility status should be determined based on age and adequacy of vaccination. For post-exposure prophylaxis, all susceptible contacts should be vaccinated within three days post exposure or receive immunoglobulin within 5 days post exposure. (See section on post-exposure prophylaxis).

Contact Tracing

Identification of contacts will depend on contact tracing. If the outbreak involves multiple cases of measles, two person teams will be assembled to interview each case, collect specimens for testing and provide on-site vaccination if indicated. If Ig is needed, that will be provided by the team as well if possible. If the number of teams required is small, they would be assembled using one local public health nurse and one regional epidemiologist from Disease Control per team. If a large number of teams are needed in the field, additional personnel may be drawn from other local public health agencies or NDDoH.

Teams would work out of the local health agency but would be under the supervision of personnel in Disease Control (which would be part of the Operations Section of the DOC). The DOC would make decisions about major investments of resources such as mass vaccination efforts or outbreak management policies.

Assistance would be provided to the teams to aid them in locating individuals and scheduling visits with persons who have been identified as contacts; likely this assistance would most effectively come from the local public health unit which will be most familiar with its communities of service. Assistance will also be provided in confirming vaccination records. This assistance will most likely come from Disease Control in Bismarck or from the DOC. The NDIIS will be the first place to look for records.¹¹ If NDIIS records are not available or incomplete, the team will need to collect information about all providers of vaccination services for each person being investigated. Those investigating vaccination history will need provider contact information to locate vaccine records. It is not necessary to obtain complete vaccination records; obtaining confirmation of the dates of vaccination for measles from providers is sufficient for outbreak response purposes. If any of those service providers are out-of-state, release of information forms should be signed at the time of interview to avoid second visits should support personnel have difficulty getting out-of-state providers to release the information.

Evaluation of Vaccination Status

Attachment 1 lists accepted evidence of immunity. ACIP has made a few modifications to this for outbreak management rather than routine vaccination. Confirmation of vaccination requires provider records or results from NDIIS or other state registry. Records held by families, although helpful, should not be considered adequate confirmation of vaccine during an outbreak. School records are suitable for vaccine coverage surveillance but should not be considered adequate for outbreak management.

¹¹ Looking in the NDIIS at the LPHU before the interview may eliminate any need to obtain detailed vaccination information during interview; however, identification of the correct person in the NDIIS needs to be certain. If insufficient information is available before the interview, a phone call to the DOC during the interview may be able to find NDIIS records and confirm measles vaccination status. If status can be found quickly, a call can be returned to the team during the interview.

Documents and Forms

Documents and forms would be provided by NDDoH to each team including:

- Interview forms
- Vaccination history forms
- Release of information forms
- Isolation and quarantine forms
- Informational documents to provide the patient or family

Containment

Disease containment depends on interrupting disease transmission by:

- Rapid identification of all persons with measles or who have been potentially exposed to measles;
- Isolation/quarantine for persons who have known or suspected measles;
- Quarantine of all persons with potential contact to a known case who do not have documentation of adequate immunity;
- Monitoring exposed individuals for illness onset;
- Vaccination of contacts who are not up-to-date on measles vaccination or use of Ig to prevent contacts from becoming ill;
- Preventing illness in health care settings by
 - Preventing uncontrolled entry of persons with febrile rash illnesses
 - Ensuring staff are fully vaccinated, and
 - Ensuring persons without up-to-date vaccination but with contraindications to vaccination are kept away from potential exposure areas.

Vaccination for Outbreak Control

General community vaccination has not been found to be an effective method for outbreak control; however, targeted vaccination of high risk populations (schools, health care institutions) is effective. Evidence of adequate immunity is defined in Attachment 4. When targeting at risk populations, those without adequate evidence of immunity should be vaccinated. For school-based vaccination, school records should not be considered adequate evidence of immunity for purposes of outbreak control. Persons who cannot demonstrate evidence of immunity should be vaccinated or excluded. Reactions to a third dose of MMR are rare, so if vaccination status is uncertain, re-vaccination is safe. Children can re-enter school immediately after receiving the vaccine. After the first dose, children still needing a second dose should receive it after 28 days. For outbreaks in healthcare institutions, all persons who can be vaccinated should have two doses of vaccine, regardless of birth year (i.e., persons born before 1957 should also be vaccinated)¹².

Children age 6 to 12 months may be vaccinated with MMR barring other contraindications. This approach is primarily used during outbreaks among children in that age groups or specific children who may be at high risk of exposure. Any child vaccinated before age 12 months will need to be re-vaccinated after 12 months which should be considered their first dose.

Vaccination Precautions

Measles vaccine is licensed in two forms in the U.S. – measles with mumps and rubella (MMR) or measles, mumps, rubella and varicella (MMRV). Monovalent vaccines are not licensed in this country.

¹² NDDoH will not necessarily consider being born in 1957 to be sufficient evidence of immunity in an outbreak setting. For instance, in a school outbreak, unvaccinated staff born before 1957 may be vaccinated.

Contraindications, precautions and potential adverse reactions to measles vaccine must consider all components of the vaccine being given, not just the measles vaccine, since all must be given together. The following cautions are noted:

- Contraindication: Anaphylactic reaction to neomycin— vaccine contains tiny amounts of neomycin
- Contraindication: Severe allergic reaction to any vaccine component
- Contraindication: Pregnancy – theoretical risk to fetus
- Contraindication: Immunosuppression
 - Cellular immunodeficiencies, hypogammaglobulinemia, dysgammaglobulinemia
 - AIDS or severe immunosuppression associated with HIV infection. Attachment 5 provides information for determining whether a person with HIV infection should be considered severely immunosuppressed.
 - Blood dyscrasias, leukemia, lymphomas of any type, or other malignant neoplasms affecting the bone marrow or lymphatic system;
 - Family history of congenital or hereditary immunodeficiency in first-degree relatives (e.g., parents and siblings), unless the immune competence of the potential vaccine recipient has been substantiated clinically or verified by a laboratory;
 - Systemic immunosuppressive therapy, including corticosteroids ≥ 2 mg/kg of body weight or ≥ 20 mg/day of prednisone or equivalent for persons who weigh >10 kg, when administered for ≥ 2 weeks.
- Precaution: Vaccination after exposure to Ig or blood transfusion (whole or packed cell) within 11 months - may interfere with generation of effective immunity in response to vaccine
- Precaution: Moderate or severe concurrent illness – Not expected to interfere with immune response but may add vaccine adverse events to current illness
- Precaution: History of thrombocytopenia or thrombocytopenic purpura – In these persons, including persons developing thrombocytopenia after prior MMR or MMRV, an acute thrombocytopenic event may be precipitated.
- Precaution: Use of TB skin test after vaccination – MMR or MMRV will interfere with normal development of a response to a TB skin test for 4 to 6 weeks. A ppd test placed prior to vaccination or at the time as vaccination will not be affected.
- Precaution: History of seizures, including febrile seizures or parent/sibling with history of seizure – MMRV appears to increase the risk of post-vaccination seizure. MMR does not have this complication.

Adverse Reaction Reporting

Adverse reactions to vaccination should continue to be collected. Reports of adverse reactions can be reported to NDDoH, where they will be entered them into VAERS, or they can be entered directly into VAERS (vaers.hhs.org) by the clinical provider. Even if entered directly into VAERS by the provider, NDDoH should be notified of any unusually severe or unusual type of adverse reaction.

Vaccine Management

Except for some Vaccines For Children (American Indian, Medicaid-eligible, uninsured, or underinsured) vaccine, NDDoH does not maintain supplies of MMR vaccine in the state for use in outbreak management. However, substantial amounts of vaccine exist in the state at the local public health and private provider level. Should additional vaccine be needed (e.g., for mass vaccination in a school), it can be ordered and will arrive quickly. When possible, vaccine shipments should go directly to the local public health unit that will be using it. If vaccine needs to come to the state, it will be managed by cold chain procedures developed by the NDDoH warehouse and transported or shipped to its point of use. (See Cold Chain plan). NDDoH can supply VFC vaccine for eligible recipients when needed. Funding to

purchase substantial quantities of vaccine are not pre-identified in Disease Control. NDDoH may receive permission from CDC to use VFC funds for outbreak control, or NDDoH may need to tap other sources in the agency to purchase vaccine (e.g., emergency response or state general funds).

Post Exposure Prophylaxis

Neither vaccination within three days of exposure nor immunoglobulin within five days of exposure is 100% effective at preventing illness onset. Estimates of protection vary from very high to very low. CDC guidance states *"If given within 72 hours of exposure to measles, measles vaccine may provide some protection."*¹³ If post-exposure vaccination can be given within 72 hours of exposure, it is preferable to immunoglobulin. Studies suggest that community contacts of cases are more likely to be protected by vaccine than household contacts. This may be because by the time many cases are identified, close contacts are likely to have been exposed for more than three days. Post-exposure immunoglobulin efficacy appears to be related to dose. Immunoglobulin concentration of measles specific antibody is lower now than in past years due to the decrease in the number of people with natural immunity contributing to the Ig pool. IGIM is limited to 15 cc, so the standard dose of 0.5cc per kg is likely to result in low titers for persons who are heavier than 30kg.

Social Distancing, Isolation and Quarantine

The public will be provided with information about how to prevent illness. Social distancing messages will likely be targeted toward those at high risk (e.g., depending on the outbreak, that might be families with children in day care or school, or persons working in a particular building). Mandatory closure of public venues is very unlikely with the possible rare exception of a school with a large number of cases. However, children from schools with one or more cases of diagnosed measles among students or staff and who are not vaccinated within 24 hours after measles is confirmed in school would need to be excluded from school until vaccinated or until 21 days after the last reported case in the school.

Protocols for isolation and quarantine, both voluntary and mandatory, can be found in a plan located in the NDDoH document library. The local health officer would be responsible for a quarantine order should that be necessary. NDDoH will provide guidance to LPH when mandatory confinement is necessary. With I&Q, whether mandatory or voluntary, comes the responsibility to ensure that persons are adequately separated from others that they may expose, including obtaining separate housing if necessary¹⁴, and ensuring that all the needs of those who in confinement are met so that they may continue in compliance with the order or recommendation (e.g., food, medicine, access to health care, clean clothing). Protocols for monitoring are included in the I&Q plan found in the NDDoH document library. The team for monitoring for illness onset among contacts and compliance with confinement may not be the same teams as those used for case investigation.¹⁵

Persons with measles would need to remain isolated for four days following onset of rash illness. Persons exposed to a known case of measles would be quarantined from day 5 to day 21 after last exposure (i.e., between the minimum and the maximum incubation period for measles). Persons under

¹³ <http://www.cdc.gov/vaccines/pubs/surv-manual/chpt07-measles.html>

¹⁴ Household member of contacts can usually be vaccinated if not immune; however, where there are contraindications to post-exposure prophylaxis or persons at high risk of serious illness (e.g., HIV) should they get ill, alternate quarters other than the case's home may be needed for the case while under isolation.

¹⁵ Roles of field team may change as the outbreak progresses and the nature of the work required changes. For instance, some teams initially assigned to contact investigation may be shifted to confinement monitoring as new contact investigation work load decreases.

quarantine would need to be monitored for onset of illness. If measles is confirmed, the person would continue in isolation until four days after rash onset.

Preventing Transmission in Health Care Settings

Because transmission of measles (and potentially other infectious diseases) can occur in both outpatient and inpatient settings, hospitals need to have plans and protocols in place for preventing transmission in health care facilities during measles outbreaks. These protocols should include the following:

- Airborne precautions and negative pressure rooms for patients admitted with measles. If a hospital does not have a negative pressure room, the patient will need to be transferred to a hospital that does.
- Triage outside of emergency rooms to identify persons with febrile rash illness who needs to be evaluated for potential measles before entering a waiting area. Persons with febrile rash illness identified outside the ER should not be cohorted together since some but not all may have measles.
- Public education to notify persons seeking health care for a febrile rash illness to call ahead to a clinic or ER and receive instructions for being seen.
- Not allowing anyone into a room occupied by a suspected measles case for two hours after the suspected case has left (due to prolonged suspension of airborne nuclei in the air after the contagious person has left the room).
- Exclusion of sick visitors from the hospital.
- Ensuring the exclusion of high risk individuals from areas of potential exposure, whether patient or employee, including all infants, pregnant women and persons with immunosuppression.

Data Management

Cases and contacts would be tracked within the MAVEN outbreak module. Cases and contacts should be entered in the system ASAP after data collection so that data is not dropped and individuals not lost to follow-up. Basic information for the line listing collected by teams should be entered into a log book rather than on a random piece of paper. The log book should include space to document that specific actions have been completed for each person in the line listing (e.g., specimen collection, vaccination of contacts, confinement). Each investigating team would need to keep a log book and transfer data into MAVEN on return to the base office. An aggregate line listing should be published on paper, updated daily and provided to each of the teams; the aggregate listing should provide basic information about each identified case and contact. Old line listings from previous days should be shredded.

In addition to a log book, a filing system needs to be maintained for all records. Each interviewed individual may have several documents or forms including clinical summaries, interview forms, vaccination forms, release of information forms and laboratory results. Records for cases and contacts should be separated and each folder clearly label as case or contact.

CDC surveillance data collection instruments are already loaded into MAVEN; however, data collection instruments may have to be modified to include North Dakota specific risk factors. If a substantial amount of data needs to be entered, managed and analyzed; Disease Control might need additional assistance from NDDoH or temporary contract personnel. Persons without advanced data skills could be used to enter information and NDDoH non-infectious disease epidemiologists or analysts from other parts of the agency may be used to assist with data management, analysis and result production. These persons could either be assigned to Disease Control or work under some other part of the incident command system in support of Disease Control.

Vaccination Data

NDIIS would be used to identify vaccination completeness. If a person is not in NDIIS or records appear incomplete, vaccination history would be obtained through provider offices. Which provider offices to contact would need to be determined from the case or contact interview. Vaccination status determination requiring calls to provider offices would likely be done in Disease Control. Additional personnel assistance may be needed for this activity.

Vaccinations given in public health offices or in provider clinics to ensure the unexposed population is up-to-date on measles vaccination would continue to be entered into NDIIS per usual practice. In the setting of a mass vaccination clinic, direct entry into NDIIS would be preferable, but may not be logistically possible in all situations. An alternative paper data collection form would be provided by Disease Control. These forms would need to be entered into NDIIS after the mass clinic either by local public health or by NDDoH.

Data Analysis and Report Production

Multiple types of data and multiple targets for data results will likely need to be managed during the outbreak. Source of data may include the following:

- Case information – data collected on investigation forms, complications, actions taken, lab results, case definition classification
- Control information – data collected on investigation form, immunity status, actions taken
- I&Q compliance data
- Surveillance data
- Intervention data (e.g., data from mass vaccination clinics)
- Policy data (e.g., school compliance with exclusion)
- Vaccine data

Targets for data would primarily be the following:

- Incident command system – Case and control line listing, epi curve, isolation and quarantine report, geographic mapping of outbreak, related out-of-state contacts, vaccine availability, surveillance report, at-risk population susceptibility/vaccine coverage, supply transport
- Agency administration
- Public information officer – Number of cases, populations at risk, hospitalizations or deaths, new cases/epi curve, geographic extent, number of persons under isolation or quarantine, progress toward disease containment
- Team in the field

Worker Protection

All persons deployed to respond to measles should use standard precautions when in contact with patients and additional precautions appropriate to the disease they are investigating.

Persons likely to be called upon to investigate a potential measles case should have written documentation of being up-to-date on MMR vaccination. Investigators born before 1957 should not be considered immune¹⁶. Vaccine immunity for measles should give excellent protection against measles;

¹⁶ If worker has not been vaccinated, they should receive the first vaccination. If they have had only one measles vaccination in the past, they should receive a second.

however, a febrile rash illness being investigated during a measles outbreak may not be measles or even vaccine preventable, but may be contagious. Case investigation of a suspected measles case should not pose substantial risk for contracting measles if the investigator is fully vaccinated, but the threshold for wearing personal protective equipment should be low. For example, an investigator who has vaccine-induced immunity against varicella (which is sometimes mistaken for measles) given ten years previously may have a uncertain risk of acquiring varicella (i.e., durability of protective antibodies following varicella vaccination is uncertain).

Persons who are needed for field response that are not up-to-date for measles vaccine must be vaccinated before they are deployed. Since some risk may exist if exposure to measles occurs immediately following first vaccination, the investigator should wear a fitted N-95 respirator for the first week post vaccination to give IgM titers a chance to rise.

Education and Training

Patient and Contact Education

Each person with measles and each contact will need to receive education. Generally the education will be performed by the team at the time the history is taken. Content of the education may include:

- Information about the disease such as manifestations and prognosis
- Incubation period post exposure
- Communicability
- Protecting family members
- Confinement procedures, legal requirements, compliance monitoring and personal rights
- Contact information to reach local public health
- Post-exposure prophylaxis including safety/risks of vaccine or Ig

Responder Training

Many of those called upon to respond to a measles outbreak will need just-in-time training related to roles that they will fill. This may include:

- Disease information
- Team function and position assignments
- Phlebotomy
- Immunity assessment and selection of vaccine or Ig for post-exposure prophylaxis
- Vaccination risk assessment
- Vaccination of young children
- Adverse reactions
- Monitoring for illness and potential for illness post prophylaxis
- Obtaining specimens for laboratory evaluation
- Interviewing
- Contact tracing
- Confinement and confinement monitoring
- Meeting the needs of those under confinement

Analyst/Assistant Training

Persons recruited to assist with data management will require some training as to specific tasks and products for which they will be responsible. Because the training requirements for some systems (e.g.,

MAVEN) are high, staff in disease control may manage aggregation of raw data and provide it to a single person responsible for allocating tasks among analysts and receiving back results.

Recovery and After Action

Several tasks will need to be completed as the outbreak winds down in North Dakota. These include:

1. Identification of source introduction – This process may be simple or complex depending on how the outbreak occurred. More extensive interviewing may be needed and coordination with CDC to track viral signature and match it up with potential sources may be necessary.
2. Missed opportunities for interdiction - As part of the after action, specific focus should be placed on where opportunities were missed to prevent or control the outbreak. This may lead to procedural or policy changes. Examples might include:
 - a. Missed contacts not found until they had become contagious
 - b. Vaccination gaps that contributed to the outbreak spread
 - c. Effectiveness or lack of effectiveness of post-exposure prophylaxis
 - d. Adequacy of protection of vulnerable persons who could not be vaccinated or who were at high risk of complications
 - e. Compliance assessment including school exclusion, I&Q compliance, health care system compliance with policies to prevent disease spread
 - f. Failures of notification particularly across state lines of possible contacts which could lead to outbreaks
 - g. Evidence of vaccine or cold chain problems (e.g., private offices or LPHU)
 - h. Unique factors or populations (e.g., oil country, hard to reach populations)
3. Opportunities for increasing vaccination coverage long term
4. Training gaps e.g., vaccine storage, case investigation and contact tracing, resources for phlebotomy or vaccination of small children

References

Manual for Surveillance of Vaccine Preventable Diseases (2011) found at <http://www.cdc.gov/vaccines/pubs/surv-manual/chpt07-measles.html>.

Prevention of Measles, Rubella, Congenital Rubella Syndrome, and Mumps, 2013: Summary Recommendations of the Advisory Committee on Immunization Practices (ACIP) (June, 2013) found at <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6204a1.htm>

Attachment 1. Acceptable Presumptive Evidence of Immunity to Measles

Routine	Students at post-high school edu. institutions	Health-care personnel[†]	International travelers
(1) Documentation of age-appropriate vaccination with a live measles virus-containing vaccine§:	(1) Documentation of vaccination with 2 doses of live measles virus-containing vaccine,§ or	(1) Documentation of vaccination with 2 doses of live measles virus-containing vaccine,§ or	(1) Documentation of age-appropriate vaccination with a live measles virus-containing vaccine:
–preschool-aged children: 1 dose	(2) Laboratory evidence of immunity,¶ or	(2) Laboratory evidence of immunity,¶ or	–infants aged 6–11 months ^{**} : 1 dose
–school-aged children (grades K-12): 2 doses	(3) Laboratory confirmation of disease, or	(3) Laboratory confirmation of disease, or	–persons aged ≥12 months§: 2 doses, or
–adults not at high risk¶¶: 1 dose, or	(4) Born before 1957	(4) Born before 1957 ^{††}	(2) Laboratory evidence of immunity,¶ or
(2) Laboratory evidence of immunity,¶ or			(3) Laboratory confirmation of disease, or
(3) Laboratory confirmation of disease, or			(4) Born before 1957
(4) Born before 1957			

[†] Health-care personnel include all paid and unpaid persons working in health-care settings who have the potential for exposure to patients and/or to infectious materials, including body substances, contaminated medical supplies and equipment, contaminated environmental surfaces, or contaminated air.

§ The first dose of MMR vaccine should be administered at age ≥12 months; the second dose of measles- or mumps-containing vaccine should be administered no earlier than 28 days after the first dose.

¶ Measles, rubella, or mumps immunoglobulin G (IgG) in serum; equivocal results should be considered negative.

^{**} Children who receive a dose of MMR vaccine at age <12 months should be revaccinated with 2 doses of MMR vaccine, the first of which should be administered when the child is aged 12 through 15 months and the second at least 28 days later. If the child remains in an area where disease risk is high, the first dose should be administered at age 12 months.

^{††} For unvaccinated personnel born before 1957 who lack laboratory evidence of measles, rubella, or mumps immunity or laboratory confirmation of disease, health-care facilities should consider vaccinating personnel with 2 doses of MMR vaccine at the appropriate interval (for measles and mumps) and 1 dose of MMR vaccine (for rubella), respectively.

¶¶ Adults at high risk include students in post-high school educational institutions, health-care personnel, and international travelers.

Source: Prevention of Measles, Rubella, Congenital Rubella Syndrome, and Mumps, 2013: Summary Recommendations of the Advisory Committee on Immunization Practices (ACIP)

Attachment 2: Classifying Suspected Measles Cases Based on Results of Case Investigation

IgM Result	Optimal time for specimen collection?*	Recent vaccination?†	Meets clinical case definition?§	Epidemiologic linkage?¶	Wild-type measles virus identified?	Case classification
+	Yes or NO	No	Yes or No	Yes or No	Yes or No	Confirmed**
+	Yes or NO	Yes	Yes	Yes	Yes or No	Confirmed
+ or -	Yes or NO	Yes or No	Yes or No	Yes or No	Yes	Confirmed
+	Yes or NO	Yes	Yes	No	No	Probable
+	Yes or NO	Yes	No	Yes or No	No	Discard
-	Yes	Yes or No	Yes or No	Yes or No	No	Discard
-	No‡	Yes or No	Yes	Yes	No	Confirmed
-	No‡	Yes or No	Yes	No	No	Probable
-	No‡	Yes or No	No	Yes or No	No	Discard

Note: Cells with "Yes or No" values do not affect the case classification.

* Optimal time for collection of IgM serum specimen is 3–28 days after rash onset.

† Receipt of measles-containing vaccine 6–45 days before rash onset.

§ Generalized maculopapular rash lasting ≥3 days and fever (>101° F or 38.3° C) and cough, coryza, or conjunctivitis.

¶ Contact with a laboratory-confirmed case (source or spread case) during the appropriate period for transmission.

** The possibility of a false-positive IgM test is increased when 1) the IgM test was not an EIA, 2) the case did not meet clinical case definition, 3) the case is an isolated indigenous case (no epidemiologic link to another confirmed case and no international travel), or 4) measles IgG was detected within 7 days of rash onset. Consider confirmatory testing for these cases.

‡ Whenever possible, collect another serum specimen 3–28 days after rash onset, conduct an IgM test, and interpret the result according to this table.

SOURCE: <http://www.cdc.gov/vaccines/pubs/surv-manual/chpt07-measles.html>

Attachment 3: Data Elements Collected for Measles Investigation

- A. Background (Cases and Contacts)
 - a. Interviewer name
 - b. County of interview
 - c. Date of interview
 - d. Case or contact interview
 - e. Earliest date reported (first notification)
- B. Demographics (Cases and Contacts)
 - a. Name
 - b. Address and county of residence
 - c. Date of birth
 - d. Age
 - e. Sex
 - f. Ethnicity
 - g. Race
- C. Clinical (Cases)
 - a. Data of symptom onset
 - b. Date of rash onset
 - c. Duration of rash
 - d. Rash presentation (location started, spread, appearance, areas of body affected or unaffected)
 - e. Symptoms
 - i. Initial
 - ii. At time of interview
 - f. Hospitalization
 - g. Complications
 - h. Outcome (live or dead)
- D. Laboratory (Cases and Contacts)
 - a. Data serology draw
 - b. Number of days after rash onset serology draw
 - c. Serological test results
 - i. Initial
 - ii. Confirmatory
 - iii. Acute /convalescent
 - d. Non-serological tests
- E. Status of Case or Contact
 - a. Confirmed Case
 - b. Probable Case
 - c. Suspected Case
 - d. Contact
- F. Interactions and Locations
 - a. Possible dates of infectivity (from 4 days before to 4 days after rash onset)
 - b. Location and interaction on each day (public and private)
 - c. Specific names and contact information for possible contacts
- G. Vaccination status (Cases and Contacts)
 - a. Number of doses of measles vaccine received
 - b. Dates of measles vaccinations
 - c. Manufacturer name
 - d. Vaccine lot number
 - e. If not vaccinated, reason
 - f. Source and certainty of vaccine history
 - g. Location of vaccination if not US
- H. Epidemiological
 - a. Transmission setting – e.g., school, workplace?
 - b. Source of infection (e.g., age, vaccination status, relationship to case)
 - c. Source of exposure (contact with probable or confirmed case, or contact with immigrants or travelers)
 - d. Import status (indigenous, international import, or out-of-state import, linked or traceable to an international importations)
 - e. Residency (Did the case reside in the U.S.?)
 - f. Travel history
 - g. Earliest possible date of exposure
 - h. Last possible date of exposure
- I. Outbreak Specific Information

[Attachment 4: Criteria for Exposure](#)

A person should be considered exposed if they:

- Have direct contact with a person with a confirmed case of measles during the period of potential infectivity.
- Sharing the same confined airspace with a person infectious with measles (e.g., same classroom, home, clinic waiting room, examination room, airplane etc.), or those in these areas up to 2 hours after the infectious person was present for even a few minutes.

For a school setting, at a minimum, classmates, roommates, team members and staff should be included among the exposed. Other venues in the school (e.g., lunch room) should be evaluated as potential sites of contact exposure.

Attachment 5: Determination of Severe Immune Deficiency in HIV

**Age-specific CD4+ T-lymphocyte count and percent of total lymphocytes
as criteria for severe immunosuppression in HIV-infected persons.**

Criteria	age <12 months	age 1-5 years	age 6-12 years	age ≥13 years
Total CD4+ T-lymphocytes	<750 per μL	<500 per μL	<200 per μL	<200 per μL
OR	OR	OR	OR	OR
CD4+ T-lymphocytes (as % of total lymphocytes)	<15%	<15%	<15%	<14%

Attachment 6: Use of Post-Exposure Immune Globulin (IG):

- Do not use with close contacts who have received 1 dose of vaccine at 12 months of age or older, unless they are immune compromised.
- IG should not be used to control measles outbreaks as immunity is temporary unless the exposure results measles infection in spite of prophylaxis. If vaccine can be given it should be given. The person receiving IG should receive measles-containing vaccine 5–6 months after IG administration or as soon thereafter as they can safely receive the vaccine.
- Dose:
 - Immunocompetent: 0.25 mL/kg body weight (maximum 15 mL), IM.
 - Immunocompromised: 0.5 mL/kg of body weight (maximum 15 mL), IM.
 - HIV Infections: Dose of Ig in HIV-infected individuals
- For those on IGIV therapy (400 mg/kg) <3 weeks before exposure, no additional IG is required.